IN THE CLAIMS

Please cancel claims 36, 40-42, 45 and 46, without prejudice or disclaimer.

Please amend claims 2-8, 10-18, 30, 33, 35, 37-39, 43, 44, 47-55, 58-61, 64 and 65 to read as follows:

--2. A recombinant allergen according to claim 1, wherein the primary mutations are spaced between about 20 to 30 Å.

3. A recombinant allergen according to claim 1 comprising a number of secondary mutations, which each reduce the specific IgE binding capability of the mutated allergen as compared to the binding capability of the said naturally occurring allergen, wherein each secondary mutation is a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, wherein the secondary mutations are placed outside the said circular region.

4. A recombinant allergen according to claim 1, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 20 %.

5. A recombinant allergen according to claim 1, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 70 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

6. A recombinant allergen according to claim 1, which essentially has the same α-carbon backbone tertiary structure as said naturally occurring allergen.

7. A recombinant allergen according to claim 1, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic genus from which said naturally occurring allergen originates.

8. A recombinant allergen according claim 1, characterised in that the specific IgE binding to the mutated allergen is reduced by at least 5%.

10. A recombinant allergen according to claim 1, characterised in that said circular surface region comprises atoms of 15-25 amino acid residues.

11. A recombinant allergen according to claim 1, characterised in that the surface-exposed amino acid residues are ranked with respect to solvent accessibility, and that one or more amino acids among the more solvent accessible ones are substituted.

12. A recombinant allergen according to claim 1, characterised in that the surface-exposed amino acid residues are ranked with respect to degree of conservation in all known homologous proteins within the species from which said naturally occurring allergen originates, and that one or more amino acids among the more conserved ones are substituted.

13. A recombinant allergen according to claim 1, wherein the mutant allergen is a non-naturally occurring allergen.

14. A recombinant allergen according to claim 1 comprising from 5 to 20 primary mutations.

15. A recombinant allergen according to claim 3 characterised in that the mutant allergen comprises from 1 to 4 secondary mutations per primary mutation.

16. A recombinant allergen according to claim 1, characterised in that one or more of the substitutions is carried out by site-directed mutagenesis.

17. A recombinant allergen according to claim 1, characterised in that one or more of the substitutions is carried out by DNA shuffling.

18. A recombinant allergen according to claim 1, characterised in that it is a mutant of an inhalation allergen.

30. A recombinant allergen according to claim 1 characterised in that it is a mutant of a venom allergen.

33. A recombinant allergen according to claim 30 characterised in that it is a mutant of Ves v 5.

35. A pharmaceutical composition comprising the recombinant allergen according to claim 1 and at least one of a pharmaceutically acceptable carrier, excipient, or adjuvant.

37. A composition comprising two or more recombinant mutant allergen variants according to claim 1, wherein each variant is defined by having at least one primary mutation, which is absent in at least one of the other variants, wherein for each variant no secondary mutation is present within a radius of 15 Å from each absent primary mutation.

38. A composition according to claim 37 comprising 2-12 variants.

39. A composition according to claim 37 further comprising at least one of a pharmaceutically acceptable carrier, excipient, or adjuvant.

43. A method of generating an immune response in a subject comprising administering to the subject a recombinant allergen according to claim 1 or a composition according to any one of claims 35, 37 or 39.

44. A method of vaccinating a subject comprising administering to the subject a recombinant allergen according to claim 1 or a composition according to any one of claims 35, 37 or 39.

47. A method for the treatment, prevention or alleviation of allergic reactions in a subject comprising administering to a subject a recombinant allergen according to claim 1 or a composition according to any one of claims 35, 37 or 39.

48. A method of preparing a recombinant allergen according to claim 1, comprising

a) identifying a number of amino acid residues in a naturally occurring allergen, which have a solvent accessibility of at least 20%;

b) selecting at least four of the identified amino acid residues in such a manner that each selected amino acid is spaced from each other selected amino acid by at least 15 Å, and that the selected amino acids are placed in such a manner that at least one circular surface region with an area of 800 $Å^2$ comprises no selected amino acid; and

c) effecting for each of the selected amino acids a primary mutation, which reduces the specific IgE binding capability of the mutated allergen as compared to the binding capability of the said naturally occurring allergen, wherein each primary mutation is a substitution of a selected amino acid residue with another amino acid, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates.

49. A method according to claim 48, characterised in ranking said identified amino acid residues with respect to solvent accessibility and substituting one or more amino acids among the more solvent accessible ones.

50. A method according to claim 48, characterised in selecting identified amino acid residues, which are conserved with more than 70 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

51. A method according to claim 50, characterised in ranking said identified amino acid residues with respect to degree of conservation in all known homologous proteins within the species from which said naturally occurring allergen originates and substituting one or more amino acids among the more conserved ones.

52. A method according to claim 48 comprising selecting the identified amino acids so as to form a mutant allergen, which has essentially the same α-carbon backbone tertiary structure as said naturally occurring allergen.

53. A method according to claim 48 characterised in that the substitution of amino acid residues is carried out by site-directed mutagenesis.

54. A method of preparing a recombinant allergen according to claim 1 comprising DNA shuffling (molecular breeding) of the DNA encoding the corresponding naturally occurring allergen to produce said recombinant allergen.

55. A DNA sequence encoding a recombinant allergen according to claim 1, a derivative thereof, a partial sequence thereof, a degenerated sequence thereof or a sequence, which hybridises thereto under stringent conditions, wherein said derivative, partial sequence, degenerated sequence or hybridising sequence encodes a peptide having at least one B cell epitope.

58. A DNA sequence according to claim 56, wherein the sequence is a derivative of the sequence shown in Fig. 3, wherein the DNA sequence encodes an allergen having at least four mutations selected from the group consisting of V2, D72, E87, K-129, E-60, N-47, K-65, P-108, N-159, D-93, K-123, K-32, D-125, R-145, D-109, E-127, Q-36, E-131, L-152, E-6, E-96, D-156, P-63, H-76, E-8, K-134, E-45, T-10, V-12, K-20, S-155, H-126, P-50, N-78, K-119, V-2, L-24, E-42, N-4, A-153, I-44, E-138, G-61, A-130, R-70, N-28, P-35, S-149, K-103, Y-150, H-154, N-43, A-106, K-115, P-14, Y-5, K-137, E-141, E-87 and E-73.

59. A DNA sequence according to claim 56, wherein the sequence is a derivative of the sequence shown in Fig. 13, wherein the DNA sequence encodes an allergen having at least four mutations selected from the group consisting of K-16, K-185, K-11, K-44, K-210, R-63, K-13, F-6, K-149, K-128, E-184, K-112, F-157, E-3, K-29, N-203, N-34, K-78, K-151, L-15, L-158, Y-102, W-186, K-134, D-87, K-52, T-67, T-125, K-150, Y-40, Q-48, L-65, K-81, Q-101, Q-208, K-144, N-8, N-70, H-104, Q-45, K-137, K-159, E-205, N-82, A-111, D-131, K-24, V-36, N-7, M-138, T-209, V-84, K-172, V-19, D-56, P-73, G-33, T-106, N-170, L-28, T-43, Q-114, C-

10, K-60, N-31, K-47, E-5, D-145, V-38, A-127, D-156, E-204, P-71, G-26, Y-129, D-141, F-201, R-68, N-200, D-49, S-153, K-35, S-39, Y-25, V-37, G-18, W-85 and I-182.

60. A DNA sequence according to claim 56, wherein the sequence is a derivative of the sequence shown in Fig. 16, wherein the DNA sequence encodes an allergen having at least four mutations selected from the group consisting of R-128, D-129, H-11, H-30, S-1, K-77, Y-75, R-31, K-82, K-6, K-96, K-48, K-55, K-89, Q-85, W-92, I-97, H-22, V-65, S-24, H-74, K-126, L-61, P-26, N-93, D-64, I-28, K-14, K-100, E-62, I-127, E-102, E-25, P-66, L-17, G-60, P-95, E-53, V-81, K-51, N-103, Q-2, N-46, E-42, T-91, D-87, N-10, M-111, C-8, H-124, I-68, P-79, K-109 and R-128, D-129, H-11, H-30, S-1, K-77, Y-75, R-31, K-82, K-6, K-96, K-48, K-55, K-89, Q-85, W-92, I-97, H-22, V-65, S-24, H-74, K-126, L-61, P-26, N-93, D-64, I-28, K-14, K-100, E-62, I-127, E-102, E-25, P-66, L-17, G-60, P-95, E-53, V-81, K-51, N-103, Q-2, N-46, E-42, T-91, D-87, N-10, M-111, C-8, H-124, I-68, P-79, K-109 and K-15.

61. An expression vector comprising the DNA according to any one of claims 55-60 operably linked to a promoter.

64. A recombinant allergen according to claim 1 comprising at least one T cell epitope capable of stimulating a T cell clone or T cell line specific for the naturally occurring allergen.

65. A diagnostic assay for assessing relevance, safety or outcome of therapy of a subject using a recombinant mutant allergen according to claim 1, comprising assessing the level of reactivity between IgE in a sample from said subject and said mutant allergen.--

Please add the following claims 66-85.

-- 66. The recombinant allergen of claim 2 wherein the primary mutations are spaced by at least 25 Å.

67. The recombinant allergen of claim 66 wherein the primary mutations are spaced by at least 30 Å.

68. The recombinant allergen according to claim 4, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 30 %.

69. The recombinant allergen according to claim 68, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 40 %.

70. The recombinant allergen according to claim 69, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 50 %.

71. A recombinant allergen according to claim 5, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 80 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

72. A recombinant allergen according to claim 71, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 90 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

73. A recombinant allergen according to claim 7, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic subfamily from which said naturally occurring allergen originates.

74. A recombinant allergen according to claim 73, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic family from which said naturally occurring allergen originates.

75. A recombinant allergen according to claim 74, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic superfamily from which said naturally occurring allergen originates.

76. A recombinant allergen according to claim 75, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic legion from which said naturally occurring allergen originates.

77. A recombinant allergen according to claim 76, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic suborder from which said naturally occurring allergen originates.

78. A recombinant allergen according to claim 77, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic order from which said naturally occurring allergen originates.

79. A recombinant allergen according claim 8, characterised in that the specific IgE binding to the mutated allergen is reduced by at least 10%.

80. A recombinant allergen according to claim 14 comprising from 6 to 15 primary mutations.

81. A recombinant allergen according to claim 80 comprising from 7 to 12 primary mutations.

82. A recombinant allergen according to claim 81 comprising from 8 to 10 primary mutations.